GLPs Related to the Development of Countermeasures

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What We'll Discuss

- Animal Efficacy Rule
- Objectives of GLPs
- GLPs in Biosecure Facilities
- Questions

Animal Efficacy Rule

- **Public Healthy Security & Bioterrorism Response Act of 2001**
  - **Section 123 - Use of animal trials in the approval of certain drugs and biologics**
    - **Required FDA to issue a final rule within six months allowing reliance on animal trials for certain priority countermeasures for public health emergencies**

Animal Efficacy Rule

- **Final Rule**
  - **67 FR 37988, 31 May 2002**
  - **Amended parts 314 & 601**
  - **Provides for approval of certain drugs & biologics based on animal data**
    - **Intended to reduce or prevent serious or life threatening conditions**

Animal Efficacy Rule

- **Adequate & well-controlled efficacy studies in humans cannot be ethically conducted**
- **Studies would involve administering a potentially lethal or permanently disabling toxic substance or organism to healthy humans**

Animal Efficacy Rule

- FDA may rely on evidence from animal studies to provide substantial evidence of the effectiveness when:
  - There is a reasonably well-understood pathophysiological mechanism of the agent & its amelioration or prevention by the product

Animal Efficacy Rule

- The effect is demonstrated in more than one animal species, unless the animal model is sufficiently well-characterized
- The animal study endpoint is clearly related to the desired human benefit

Animal Efficacy Rule

- **The pharmacokinetics and phamacodynamics of the product in animals & humans are sufficiently well-understood to be able to select an effective dose in humans**

Animal Efficacy Rule

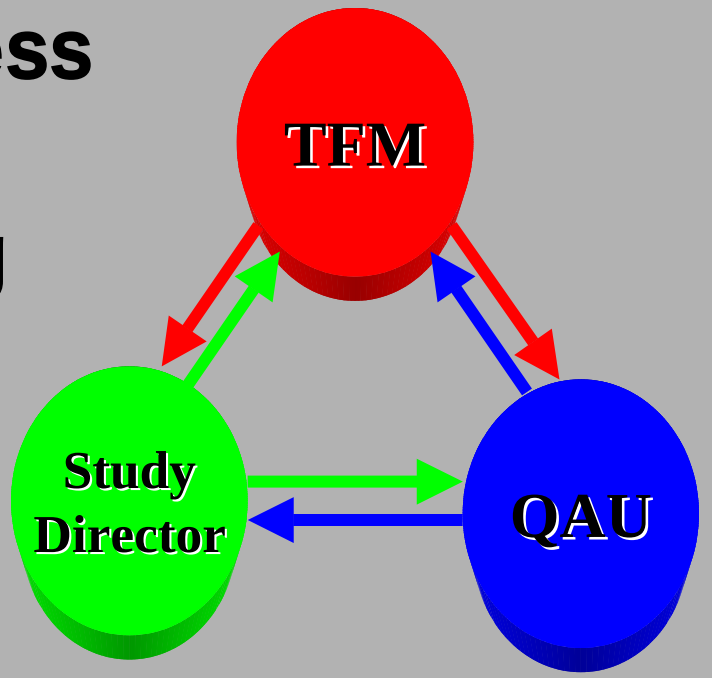
- **All studies subject to this rule must be conducted in accordance with preexisting under the good laboratory practice (21 CFR 58) regulations and the Animal Welfare Act (7 U.S.C. 2131)**

Animal Efficacy Rule

- **Conforming amendment to GLPs**
  - **Revise the definition of nonclinical laboratory to encompass animal efficacy studies**
  - **Will be published as a direct final rule**
  - **Currently in agency clearance**

Objectives of GLPs

- GLPs are designed as a quality management system intended to ensure the quality and integrity of nonclinical laboratory studies
- Inspectional process focuses on the proper functioning of the quality system



Objectives of GLPs

- **Testing facility management involvement is the most critical factor in achieving GLP compliance**
- **Management's role in the quality system may be heightened in a secure testing environment**

Objectives of GLPs

- Permit the reconstruction of study events and verification of the final report independent of personnel that conducted the study
- Accomplished through inspection of raw data, specimens, records, and other documentation

GLPs in Secure Facilities

- **Management Responsibilities**
  - **Determine if they have qualified personnel, facilities, and equipment to conduct studies in compliance with GLPs**
  - **Assure that training and procedures are for specialized techniques are available**
  - **Assure test articles are tested for strength, identity, strength, purity, stability, and uniformity**

GLPs in Secure Facilities

- **Management Responsibilities**
  - **Accommodate additional/different demands on study directors, personnel, and QAU**
  - **Accommodate internal (QAU) and external inspections of secure areas as necessary**

GLPs in Secure Facilities

- **Study Director Responsibilities**
  - **Must assure that they continue as the single point of study control**
    - **Communication**
    - **SOPs**
    - **Protocol amendments**
  - **Must assure that are accurately recorded and verified**
    - **Non-traditional recording methods**
    - **Verification within and outside barrier**

GLPs in Secure Facilities

- **Study Director Responsibilities**
  - **Must assure there are methods to document and communicate corrective actions**
  - **Continue to assure that all GLP regulations are followed**

GLPs in Secure Facilities

- **QAU Responsibilities**
  - **Personnel qualified to conduct inspections in secure areas**
  - **Explore the use of alternative methods to conduct inspections and audits**
  - **Appraise management of the affect that secure facilities has on the scheduling, conduct, and time requirements for conducting inspections and audits**

Article Characterization

- GLPs require that each batch of article be appropriately defined
  - Identity
  - Strength
  - Purity
  - Composition
  - Other characteristics

Article Characterization

- The testing necessary to appropriately define articles used in studies evaluating counter-terrorism agents may rely heavily on the “other characteristics”
- What the other characteristics are is a scientific issue and needs to be discussed with FDA review divisions

GLPs in Secure Facilities

- **Raw data**
  - **Raw data collected within a secure area may be damaged or destroyed during decontamination**
    - **GLPs permit the substitution of an exact copy (verbatim and verified accurate by signature) for the original source as raw data**
    - **Procedures and training for verification process**

GLPs in Secure Facilities

- **Raw data**
  - **Non-traditional recording of raw data**
    - **Special materials for written records**
    - **Video and audio tapes**
    - **Electronic data**
  - **Assure non-traditional recording methods permit records to be retained for required period**

GLPs in Secure Facilities

- Maintenance and calibration of equipment
  - May require management to expend additional resources for additional redundancy
  - Study directors need to assure that equipment calibration schedule do not conflict with study schedule

GLPs in Secure Facilities

- **Facility requirements**
  - **By their nature secure facilities should readily be able to comply with requirements for:**
    - **Isolation of projects**
    - **Isolation of biohazardous materials**
    - **Quarantine of animals**
    - **Preventing mix-ups with test or control articles**

Questions?

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